NAPM

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October 26, 1999

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 85N-0214, 180-Day Generic Drug Exclusivity

Dear Food and Drug Administration:

This comment is submitted by the National Association of Pharmaceutical Manufacturers, in response to the proposed rule published in the Federal Register for August 6, 1999. 64 Fed. Reg. at 42,873. NAPM is the national, not-for-profit trade association representing generic drug manufacturers and suppliers of bulk active drug substances and related goods and services to the pharmaceutical industry.

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With the exception of several specific matters discussed below, NAPM agrees with FDA's proposed rule, and urges FDA to publish a final rule as soon as reasonably possible. Prompt publication of a final rule will provide certainty to NAPM's members and the rest of the pharmaceutical industry. It will also benefit American consumers, taxpayers, and third-party payors by speeding the availability of generic versions of brand name drug products. Under FDA's current approach of regulating directly from the statute on a case-by-case basis, there is a distinct possibility that the market for generic versions of a particular brand name drug product will be blocked indefinitely because the generic applicant entitled to 180-day exclusivity either cannot, or chooses not to, market its generic product. When the generic market can be blocked indefinitely by a 180-day exclusivity period that does not start running, the only certain "winner" is the brand name drug manufacturer that enjoys an extended monopoly. That situation does not promote the public health and could not have been intended by Congress when it passed the Hatch-Waxman Amendments in 1984.

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In particular, NAPM supports FDA's tentative decision to use a "triggering period" to prevent indefinite blockage of the generic market. NAPM believes the 180-day exclusivity "reward" is an important incentive for generic drug manufacturers to engage in necessary research and development, as well as to defend against costly patent infringement litigation that is often necessary if a generic drug product is to be marketed before the expiration of a patent listed in the Orange Book. In most cases, the proposed 180-day triggering period represents an appropriate balance between, on the one hand, the rights of the generic drug applicant entitled to 180-day exclusivity and, on the other hand, the rights of competing generic drug manufacturers and the public interest. NAPM also supports the special 60-day triggering period that would apply if the firm entitled to 180-day exclusivity has already received final approval at the time the triggering period begins, and either has not been sued for patent infringement as a result of its paragraph IV certification, or has been sued and the case was settled or dismissed without a decision on the merits of the patent claim.

* * *

FDA proposed to retain the longstanding requirement that the applicant that submits the first substantially complete paragraph IV ANDA is entitled to 180-day exclusivity. Under the proposal, FDA would continue to require that a "substantially complete" ANDA contain all information required by FDA's regulations, including but not limited to any required bioequivalence study.

NAPM understands that FDA currently purports to give increased scrutiny to the first paragraph IV ANDA. However, NAPM does not believe that level of scrutiny is sufficient and requests that FDA scrutinize the first paragraph IV ANDA even more carefully. FDA should focus on the bioequivalence study and stability data, as well as all other areas where FDA has historically found problems with ANDAs. Specifically, before accepting the first paragraph IV ANDA for filing, FDA should determine that all key bioequivalence parameters in the ANDA meet agency standards for confidence intervals, and that all stability data are within product specifications. If, based on this further-increased level of scrutiny, FDA determines that the first paragraph IV ANDA submitted to the agency is not substantially complete and, therefore, cannot be received for filing, then the next-submitted paragraph IV ANDA applicant that is found to be substantially complete on the basis of an increased level of scrutiny should be eligible for the 180-day exclusivity.

NAPM's concern is that a generic firm may intentionally file a paragraph IV ANDA that, under the current degree of scrutiny to determine acceptability for filing, appears to be acceptable for filing, but in fact falls short of meeting the substantive standards for approval. For example, a generic firm could intentionally submit a paragraph IV ANDA with a bioequivalence study that appears to be complete, but that the firm knows to be deficient, for the sole purpose of denying 180-day exclusivity to a competitor that is expected to be ready soon thereafter to submit an acceptable paragraph IV ANDA. The increased level of scrutiny that we request will help eliminate this potential for gaming the system.

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The rulemaking preamble states that the applicant that submits the first substantially complete paragraph IV ANDA would lose its eligibility for 180-day exclusivity if it is required to submit a new bioequivalency study. The rulemaking preamble also states: "In addition, if the first applicant submits a new paragraph IV certification because, for example, it makes a formulation change requiring a supplement or an amendment to its ANDA, it may no longer be accorded first applicant status." 64 Fed. Reg. at 42,875. NAPM interprets these statements as meaning that the only types of amendments to a pending ANDA that would lead to loss of eligibility for 180-day exclusivity are: (i) the submission of a new bioequivalence study, and (ii) formulation changes that require a new paragraph IV certification. NAPM requests that the preamble to the final rule address whether NAPM's understanding is correct. NAPM also requests that FDA address when a formulation change requires a new paragraph IV certification.

By using the term "supplement" in the preamble language quoted in the previous paragraph, FDA apparently contemplates that, in some cases, a supplement to an approved paragraph IV ANDA may trigger a new paragraph IV certification and the loss of 180-day exclusivity. NAPM requests that FDA elaborate on this situation and set forth, in as much detail as possible, examples of circumstances that will, and will not, lead to loss of eligibility for 180-day exclusivity. NAPM also requests that FDA address both pending and approved ANDAs.

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FDA proposed to amend § 314.107(c)(1) so that the first paragraph IV ANDA applicant would be eligible for 180-day exclusivity even if that applicant is not sued for patent infringement. NAPM urges FDA to reconsider that tentative conclusion and to conclude that the first paragraph IV ANDA applicant is eligible for 180-day exclusivity only if sued for patent infringement. In the preamble to its 1989 proposed rule to implement 180-day exclusivity and other ANDA provisions, FDA stated:

> Section 505(j)(4)(B)(iv)[1] can thus be applied straightforwardly only when an applicant who seeks the 180-day period of exclusive marketing has been involved in a patent infringement lawsuit. To apply the section where there has been no lawsuit, requires either that the agency ignore the plain language of the section, essentially reading out the phrase "first commercial marketing," or that the agency assume, contrary to the goals of the 1984 Amendments, that Congress intended to create an incentive for delay in competition, without any countervailing benefit to society. Moreover, the policy embodied in the provision, of rewarding the applicant who devotes the considerable time and money necessary for patent litigation, is not served by providing 180 days of exclusive marketing to an applicant who avoids a lawsuit. Accordingly, proposed § 314.107(c) applies only when the first applicant has been sued. [footnote omitted]

54 Fed. Reg. 28,872, 28,894-95 (July 10, 1989).

After reviewing the comments received, FDA did not change its conclusion in any way. In the preamble to the 1994 final rule, FDA stated:

> Section 505(j)(4)(B)(iv) of the act can be applied straightforwardly only when an applicant who seeks the 180-day period of exclusive marketing has been involved in a patent infringement lawsuit. To apply the section where there has been no lawsuit would require that the agency ignore the textual relationship between section 505(j)(4)(B)(iii) and (j)(4)(B)(iv) of the act and assume that Congress intended, contrary to the goals it stated in the legislative history, to create an incentive for delay in generic competition, without any countervailing benefit to society. Moreover, it would provide a windfall to an applicant who has not devoted the considerable time and money necessary for patent litigation. Thus, consistent with the agency's longstanding interpretation of the act, § 314.107(c) applies only when the first applicant has been sued. Although, as the comments state, one Federal district court reached a contrary conclusion, the agency appealed that decision and, on appeal, the decision was vacated as moot. [citation omitted] The agency has not altered its interpretation of the act.

59 Fed Reg. 50,338, 50,353 (October 3, 1994).

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[1] Former section 505(j)(4) is now codified as section 505(j)(5).

The reasons articulated by FDA in 1989 and 1994 to support the "must be sued" requirement for 180-day exclusivity remain valid today. To support its current change in position, FDA cites just two factors. The first factor is judicial invalidation of the "successful defense" requirement. But there is no tie of any kind between the "successful defense" and the "must be sued" requirements. In its 1994 rulemaking preamble, FDA discussed these matters in separate -- and totally distinct -- portions of the preamble. See 59 Fed. Reg. at 50,352-53 ¶¶ 72 ("must be sued") and 76 ("successful defense"). The structure of the discussion illustrates that there is no textual or logical link between the "must be sued" and the "successful defense" requirements. Second, FDA cited "subsequent reconsideration of the statutory language" as a basis for abandoning the longstanding "must be sued" requirement. 64 Fed. Reg. at 42,876. However, in the current rulemaking preamble, FDA also states: "The agency recognizes that neither the *Purepac* nor the *Mova* opinion expressly foreclosed the agency from adopting a requirement that an applicant be sued." Id. NAPM agrees with that statement. The policy and statutory interpretation reasons relied upon by FDA in 1989 and 1994 for adopting the "must be sued" requirement are unchanged today. In the current rulemaking preamble, FDA simply states that a first applicant that is able to "design around" an Orange Book patent and avoid patent litigation altogether should be entitled to 180-day exclusivity. There is no discussion explaining why the agency has done an abrupt about-face on its 1989 and 1994 positions, which remain valid today. NAPM believes there is no sound explanation for the agency's change in position. Therefore, NAPM urges that the final rule include a "must be sued" requirement for 180-day exclusivity.

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Proposed 21 C.F.R. § 314.107(e) and the rulemaking preamble, 64 Fed. Reg. at 42,881, would allow a firm entitled to 180-day exclusivity to waive its exclusivity in favor of one or more specific firms only if the commercial marketing trigger or the court decision trigger has taken place; in the absence of a triggering event, the applicant entitled to 180-day exclusivity would only be able to relinquish its exclusivity entirely. NAPM urges FDA to allow the selective waiver of exclusivity, whether or not a triggering event has taken place.

In some cases, allowing the selective waiver of 180-day exclusivity before a triggering event has taken place can speed the availability of generic competition, thereby helping fulfill the intent of the Hatch-Waxman Amendments. Moreover, as FDA has recognized and actual industry experience has shown, 180-day exclusivity is a valuable property right. In many cases, that property right will be worth more if exclusivity can be waived selectively, rather than being relinquished all together. There is no reason why an applicant entitled to 180-day exclusivity should not receive the full benefit of its property right, regardless of whether a triggering event has taken place.

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NAPM urges the agency to publish a final rule as soon as possible. The final rule should be based on the proposed rule, with the changes suggested above. NAPM appreciates this opportunity to comment.

Sincerely yours,

Robert S Milanese

Robert S. Milanese
President